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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/147,036

12/15/1998

JOCHEN MAURER

P564-8019

1165

6449

7590

10/20/2005

ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER

FORD, VANESSA L

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 10/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/147,036

Applicant(s)

MAURER ET AL.

Examiner

Vanessa L. Ford

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 August 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,9-15,19,41,43-53 and 55-57 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,9-15, 19,41,43-53 and 55-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 July 2004 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 3, 2005 has been entered. Claims 1, 15, 41, 55 and 57 have been amended.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 41 and 43-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling a process for presenting a passenger peptide or polypeptide on the surface of a gram-negative host bacteria does not enable a process for presenting a passenger peptide or polypeptide on the surface of all host bacteria wherein the passenger peptide or polypeptide is modified by glycosylation.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification teaches that various procedures according to the invention are conceivable for expressing functional antigen-binding parts of antibodies which are not

Art Unit: 1645

usually glycosylated on the surface of gram-negative bacteria, preferably *E. coli* (page 14). Example 2 of the instant specification teaches the construction of a surface-exposed fusion protein having an antigenic determinant as passenger protein (page 33). The Example uses cholera toxin subunit B as the passenger protein (page 34). Example 3 of the instant specification teaches the construction of a surface-presented peptide fusion on the surface of a gram-negative bacteria. The instant specification has failed to teach how the fusion peptide produced in Example 3 is glycosylated.

The state of the art regarding glycosylation in gram-negative bacteria is cited below.

Schaffer et al (*Biochemie* 83, 2001, pages 591-599) teach that prokaryotes synthesizing glycoproteins are pathogens from the genera *Neisseria*, *Mycobacterium*, *Streptococcus* and *Campylobacter* (page 591). Schaffer et al teach that it is important to determine how and where prokaryotic protein glycosylation takes place and how it is regulated at the molecular level (page 591).

Benz et al (*Molecular Microbiology*, 2002, 45(2), p. 267-276) teach that a few eubacteria can express glycoproteins (see the Abstract). However, Benz et al teach that the complexity and variability of prokaryotic protein glycosylation is quite apparent (page 273). Benz et al teach that the organization and localization of components of the general glycosylation system of prokaryotes is unknown (page 273). Benz et al teach that some prokaryotic proteins are glycosylated by enzymes and others glycosylated by their own glycosylation island (page 273). Benz et al teach that there are many unanswered questions regarding prokaryotes and glycosylation. Benz et al

Art Unit: 1645

teach a number of unanswered question include: What are the components of the glycosylation machinery? Can a substrate consensus sequence be defined? What are the components of the glycosylation machinery in different bacteria? Are glycosylation islands found in many bacteria species? Is heterologous glycosylation in recombinant strains possible?

Factors to be considered in determining whether undue experimentation is required are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

The cited art has taught that glycosylation does occur in some gram-negative bacteria. However, the cited art teaches that the components of the glycosylation machinery and how this machinery differs in different bacteria is unknown. The prior art has only made a correlation between glycosylation and a few genera of bacteria. It should be noted that the claimed process encompasses the expression of any bacteria. The cited art suggests that all bacteria do not glycosylate proteins. In fact, the cited art teaches that if a bacteria glycosylates proteins different mechanisms can be used to glycosylate proteins. The cited art is also uncertain that heterologous glycosylation in recombinant strains can be achieved. One of skill in the art would not reasonably conclude from the teachings of the prior art that glycosylation can be achieved in all bacteria that are encompassed by the claimed process.

Art Unit: 1645

In view of the lack of guidance in the instant specification and the art, it is determined that a skilled artisan is forced into undue experimentation to practice (make and use) the invention as is broadly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. The following claims are rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claims 1, 9-15, 29 and 55-57 recite "...wherein the nucleotide sequence encoding the transport domain is located downstream from the nucleotide sequence encoding the passenger peptide or polypeptide". What is Applicant referring to since a vector or plasmid can be circular and therefore no downstream or upstream orientation is possible. Clarification is required.

b) Claim 41 and 43-53 (claim 49 in particular) recite "...wherein the modification is a glycosylation..." It is unclear as to where the peptide or polypeptide is glycosylated. At what point in the process of claim 41 does this modification or glycosylation occur? Clarification is required.

Art Unit: 1645

c) Claims 41, 43-53 and 55-57 recite "... a process for obtaining a library of bacteria expressing a variant population of surface exposed passenger peptides or polypeptides..." Are all peptides or polypeptides expressed by the same vector, at the same time or is the process repeated to generate multiple individual peptides and polypeptides? Clarification is required.

d) Claims 41, 43-53 and 55-57 recite "...g) identifying and characterizing a binding partner for the surface-exposed passenger peptide or polypeptide..." . It is unclear as to what Applicant is referring. Are the identification and characterization steps required in the process of expressing the passenger peptide or polypeptide to the surface or is the passenger peptide or polypeptide known in the claimed process of expression? Clarification is required.

Status of Claims

4. No claims are allowed.

Art Unit: 1645

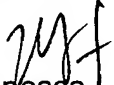
Conclusion

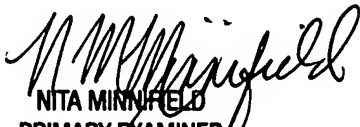
5. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Vanessa L. Ford
Biotechnology Patent Examiner
October 13, 2005


NITA MINNIFIELD
PRIMARY EXAMINER
10/17/05